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EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 10/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/054,638	RYALL, ROBERT P.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-36,46,48-52,54,56 and 57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-36,46,48-52,54,56 and 57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

Applicant's Amendment

1) Acknowledgment is made of Applicant's amendment filed 06/07/05 in response to the final Office Action mailed 12/07/04. With this, Applicant has amended the specification.

Status of Claims

2) Claims 37-45, 47, 53 and 55 have been canceled via the amendment filed 06/07/05.

Claims 18-33, 35, 48, 50 and 52 have been amended via the amendment filed 06/07/05.

Claims 18-36, 46, 48-52, 54, 56 and 57 are pending and are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Specification

5) The specification as amended via the amendment filed 06/07/05 is objected to under 35 U.S.C. § 132, because it introduces new matter into the disclosure. 35 U.S.C. § 132 states that no amendment shall introduce new matter into the disclosure of the invention.

The limitation(s) added at paragraph [0033]: 'R1005 (N-2-Deoxy-2-L-leucylamino .....hydroacetate', '(3-.....cholesterol)', (e.g., Poly[bis(carboxylatophoxy)phosphazene] and/or Poly[di(carboxyatophoxy)phosphazene])', '(oligodeoxynucleotide motifs), saponin adjuvants e.g., (QS-7' is new matter. Neither the generic limitation 'saponin adjuvants', nor the narrower limitation 'QS-7' are supported in the specification, as originally filed. The current exemplication for 'pcpp': '(e.g., Poly[bis(carboxylatophoxy)phosphazene] and/or Poly[di(carboxyatophoxy)phosphazene])' is new matter. No authoritative source, such as, a standard textbook or a commercial catalogue that equates the recited trademark or abbreviated adjuvants to the newly added generic descriptions, is provided to establish that what is now added does not constitute new matter.

Rejection(s) Moot

6) The rejection of claims 53 and 55 made in paragraph 17 of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, first paragraph, as containing new subject matter, is moot in light of Applicant's cancellation of the claims.

7) The rejection of claims 37-45, 47, 53 and 55 made in paragraph 14(f) of the Office Action mailed 01/07/04 and made/maintained in paragraph 15 of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicant's cancellation of the claims.

8) The rejection of claims 38-45 made in paragraph 18 of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, first paragraph, as containing new subject matter, is moot in light of Applicant's cancellation of the claims.

9) The rejection of claim 47 made in paragraph 19 of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, first paragraph, as containing new subject matter, is moot in light of Applicant's cancellation of the claim.

10) The rejection of claim 37 made in paragraph 20(q) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicant's cancellation of the claim.

11) The rejection of claims 39, 41, 43 and 45 made in paragraph 20(r) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicant's cancellation of the claims.

12) The rejection of claims 38-45 made in paragraph 20(s) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicant's cancellation of the claims.

13) The rejection of claims 37-45, 47, 53 and 55 made in paragraph 20(v) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicant's cancellation of the claims.

14) The rejection of claim 37 made in paragraph 21 of the Office Action mailed 12/07/04 under 35 U.S.C. § 102(b) as being anticipated by Chong *et al.* (WO 99/42130, already of record), is moot

in light of Applicant's cancellation of the claim.

15) The rejection of claim 47 made in paragraph 23 of the Office Action mailed 12/07/04 under 35 U.S.C. § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10: 691-698, 1992, already of record) and McMaster (6,146,902 – Applicants' IDS submitted 07/07/04) in view of Andre *et al.* (*In*: *Modern Vaccinology*. (Ed) Kurstak *et al.* Plenum Medical Book Company, New York, pp. 41-54, 1994, already of record); Levine *et al.* (*In*: *Abstracts of the Tenth International Pathogenic Neisseria Conference*, (Ed) Zollinger *et al.* Baltimore, USA, pages 228-230, November, 1997, already of record) and Lindberg AA (*Vaccine* 17: S28-S36, 1999 – Applicants' IDS), is moot in light of Applicant's cancellation of the claim.

16) The rejection of claim 37 made in paragraph 24 of the Office Action mailed 12/07/04 under 35 U.S.C. § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10: 691-698, 1992, already of record) and McMaster (6,146,902 - Applicants' IDS submitted 07/07/04) as modified by Andre *et al.* (*In*: *Modern Vaccinology*. (Ed) Kurstak *et al.* Plenum Medical Book Company, New York, pp. 41-54, 1994, already of record); Levine *et al.* (*In*: *Abstracts of the Tenth International Pathogenic Neisseria Conference*, (Ed) Zollinger *et al.* Baltimore, USA, pages 228-230, November, 1997, already of record) and Lindberg AA (*Vaccine* 17: S28-S36, 1999 – Applicants' IDS) as applied to claims 35, 34 and 18 above, and further in view of Petre *et al.* (US 6,013,264), is moot in light of Applicant's cancellation of the claim.

17) The rejection of claims 38-45 made in paragraph 24 of the Office Action mailed 12/07/04 under 35 U.S.C. § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10: 691-698, 1992, already of record) and McMaster (6,146,902 - Applicants' IDS submitted 07/07/04) as modified by Andre *et al.* (*In*: *Modern Vaccinology*. (Ed) Kurstak *et al.* Plenum Medical Book Company, New York, pp. 41-54, 1994, already of record); Levine *et al.* (*In*: *Abstracts of the Tenth International Pathogenic Neisseria Conference*, (Ed) Zollinger *et al.* Baltimore, USA, pages 228-230, November, 1997, already of record) and Lindberg AA (*Vaccine* 17: S28-S36, 1999 – Applicants' IDS) as applied to claims 33 and 18 above, and further in view of Jennings *et al.* (US 5,811,102) ('102), is moot in light of Applicant's cancellation of the claims.

18) The rejection of claims 53 and 55 made in paragraph 26 of the Office Action mailed 12/07/04 under 35 U.S.C. § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10: 691-

698, 1992, already of record) and McMaster (6,146,902 - Applicants' IDS submitted 07/07/04) as modified by Andre *et al.* (*In*: *Modern Vaccinology*. (Ed) Kurstak *et al.* Plenum Medical Book Company, New York, pp. 41-54, 1994, already of record), Levine *et al.* (*In*: *Abstracts of the Tenth International Pathogenic Neisseria Conference*, (Ed) Zollinger *et al.* Baltimore, USA, pages 228-230, November, 1997, already of record) and Lindberg AA (*Vaccine* 17: S28-S36, 1999 – Applicants' IDS) as applied to claim 51, 33 and 18 above, and further in view of Avendano *et al.* (*Pediatric Infect. Dis. J.* 12: 638-643, 1993), is moot in light of Applicant's cancellation of the claims.

Rejection(s) Withdrawn

19) The rejection of claim 18 made in paragraph 14(b) of the Office Action mailed 01/07/04 and maintained in paragraph 14 of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the claim.

20) The rejection of claims 19-33, 34-36, 46, 48-52, 54, 56 and 57 made in paragraph 14(f) of the Office Action mailed 01/07/04 and made/maintained in paragraph 15 of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the base claim.

21) The rejection of claim 18 made in paragraph 20(a) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn. A modified rejection is set forth below.

22) The rejection of claims 20, 21, 23, 24 and 25 made in paragraph 20(b) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the claims.

23) The rejection of claim 52 made in paragraph 20(c) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the claim.

24) The rejection of claims 18, 26, 29 and 33 made in paragraph 20(d) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the claims.

25) The rejection of claims 20 and 21 made in paragraph 20(e) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the claims.

26) The rejection of claim 22 made in paragraph 20(f) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the claim.

27) The rejection of claims 27-32 made in paragraph 20(g) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the claims.

28) The rejection of claim 26 made in paragraph 20(i) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the claim.

29) The rejection of claim 29 made in paragraph 20(j) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the claim.

30) The rejection of claim 33 made in paragraph 20(k) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the claim.

31) The rejection of claim 26 made in paragraph 20(l) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the claim.

32) The rejection of claim 29 made in paragraph 20(m) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the claim.

33) The rejection of claim 33 made in paragraph 20(n) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the claim.

34) The rejection of claim 35 made in paragraph 20(o) of the Office Action mailed 12/07/04

under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the claim.

35) The rejection of claim 36 made in paragraph 20(q) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the claim.

36) The rejection of claims 18 and 48 made in paragraph 20(t) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the claims.

37) The rejection of claim 48 made in paragraph 20(u) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the claim.

38) The rejection of claims 19-36, 46, 48-52, 54, 56 and 57 made in paragraph 20(v) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendments to the base claim.

39) The rejection of claim 35 made in paragraph 20(p) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendments to the claim.

40) The rejection claims 18-33 made in paragraph 15 of the Office Action mailed 01/07/04 and maintained in paragraph 16 of the Office Action mailed 12/07/04 under 35 U.S.C. § 102(b) as being anticipated by Chong *et al.* (WO 99/42130), is withdrawn in light of Applicant's amendment to the base claim.

41) The rejection of claims 34-36, 46, 51 and 54 made in paragraph 21 of the Office Action mailed 12/07/04 under 35 U.S.C. § 102(b) as being anticipated by Chong *et al.* (WO 99/42130, already of record), is withdrawn in light of Applicant's amendment to the base claim.

Rejection(s) Maintained

42) The rejection of claim 26 made in paragraph 20(h) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is maintained for reasons set forth therein. The claim continues to refer to serogroup A or serogroup C as 'serogroups' as opposed to

--serogroup--.

43) The rejection of claims 49 and 50 made in paragraph 20(t) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is maintained for reasons set forth therein.

Applicant contends that he has amended claims 48-50 to delete the term 'derived'. However, claims 49 and 50 still include the limitation 'derived'. The rejection stands.

44) The rejection of claim 19 made in paragraph 20(b) of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is maintained for reasons set forth therein. The claim as amended, does not, include the suggested amendment and continues to have the limitation, 'from *N. meningitidis* serogroup ..'.

45) The rejection of claims 52 and 54 made in paragraph 17 of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, first paragraph, as containing new subject matter, is maintained for reasons set forth therein.

Applicant contends that claims 52 and 54 are supported by the specification in numerous places including pages 38-45. Applicant reproduces a portion of the specification from page 38 and states that this part of the specification provides support for sterile liquid preparations administered in various injectable formulations and methods. Applicant states that the specification incorporates the well-respected treatise *Remington's Pharmaceutical Science* 17th (1985) by reference, and that those skilled in the pharmaceutical, vaccine, and human therapeutics arts readily recognize this treatise as providing detailed information on the formulation, administration and dosing of human therapeutics. Applicant contends that the specification and the treatise incorporated therein provide sufficient support for the claims. Applicant asserts that MPEP does not require verbatim recitation in the specification of any newly added claim terms. MPEP 2163(I)(B) is stated as acknowledging that newly added claim terms can be 'supported in the specification through express, implicit, or inherent disclosure'. Applicant opines that *In re Rasmussen* is not dispositive on the issue.

Applicant's arguments have been carefully considered, but are not persuasive. Applicant is correct in that claim limitations can be supported in the specification through express, implicit, or inherent disclosure. Applicant is also correct in that the specification teaches sterile liquids. However, the claim limitation at issue is a structural limitation, which recites that the sterile liquid

is 'contained within a single use syringe' or 'contained within a vial'. With regard to the treatise, the specification states that standard texts 'such as' 'REMINGTON'S PHARMACEUTICAL SCIENCE, 17th edition, 1985, incorporated herein by reference, 'may' be consulted 'to prepare suitable preparations' without undue experimentation. The recitation in the specification with regard to REMINGTON'S PHARMACEUTICAL SCIENCE is limited to 'preparing suitable preparations' which does not provide descriptive support, or express, implicit, or inherent disclosure for the now added structural claim limitations that are identified above. The rejection stands.

46) The rejection of claim 48 made in paragraph 19 of the Office Action mailed 12/07/04 under 35 U.S.C. § 112, first paragraph, as containing new subject matter, is maintained for reasons set forth therein and herebelow.

Applicant states that he has replaced the term 'organism' with the term 'bacterium' and amended claim 48 to now depend from claim 46.

Applicant's argument has been carefully considered, but is not persuasive. Claim 48, as amended, still encompasses an inactivated bacterial toxin other than tetanus toxoid from *Clostridium tetani*, diphtheria toxoid and CRM197 from *Corynebacterium diphtheriae,* pertussis toxoid from *Bordetella pertussis*, exotoxin A from *Pseudomonas aeruginosa*, LT and ST from *Escherichia coli*, which are not described in the specification, as originally filed. See lines 9-11 on page 5 of the specification. For instance, *Bordetella pertussis* produces several toxins other than pertussis toxin (PT or LPF), such as, endotoxin (LPS), adenylate cyclase toxin, heat-labile toxin, tracheal cytotoxin, dermonecrotic toxin, and haemolytic toxin etc. However, inactivated forms of toxins of such a broad scope are not supported in the instant specification. The rejection stands.

47) The rejection of claims 18-33 and 51 made in paragraph 22 of the Office Action mailed 12/07/04 under 35 U.S.C. § 103(a) as being unpatentable over McMaster (6,146,902 – Applicants' IDS submitted 07/07/04) in view of Andre *et al.* (*In*: *Modern Vaccinology*. (Ed) Kurstak *et al.* Plenum Medical Book Company, New York, pp. 41-54, 1994, already of record), Levine *et al.* (*In*: *Abstracts of the Tenth International Pathogenic Neisseria Conference*, (Ed) Zollinger *et al.* Baltimore, USA, pages 228-230, November, 1997, already of record) and Lindberg AA (*Vaccine* 17: S28-S36, 1999 – Applicants' IDS), is maintained for reasons set forth therein and herebelow.

Applicant cites MPEP 2143 and states that a valid *prima facie* case of obviousness exists

when the Office establishes three criteria: some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; a reasonable expectation of success; and teaching or suggestion of all the claim limitations by the prior art reference or references when combined. Applicant cites case law and further submits the following arguments: (a) The cited references at best provide a motivation to try to develop efficacious combinations of two, three, or four distinct separately made protein-capsular polysaccharide conjugates as are presently being claimed. (b) The Office failed to address the Applicant's previous 'obvious to try' remarks submitted via the paper mailed 09/08/04. (c) Unrebutted are the Applicant's remarks that given the disclosure of Granoff WO 98/58670, cited in the Office Action mailed 01/07/04, one skilled in the art would not expect to successfully make and administer multivalent/tetravalent combination of protein-capsular polysaccharide conjugates comprising meningococcal serogroups W-135 and Y. (d) The Federal Circuit has repeatedly held that using an 'obvious to try' rational is a legally impermissible basis for attempting to establish a motivation to combine references especially in unpredictable fields such a immunology and vaccinology. (e) Levine *et al.* describe a hypothetical cost-effectiveness decision model and focus on the as yet unrealized public health benefits of the hypothetical successful concomitant vaccination of infants with a tetravalent *N. meningitidis* polysaccharide-protein conjugate vaccine and a Hib conjugate vaccine in the same syringe as a means of decreasing costs associated with meningococcal disease. There was no data cited to support the analysis forcing the authors to make several unsupported assumptions. (f) Andre *et al.* state that a number of non-conjugated vaccines and immunogenic compositions could potentially be effective against disease caused by *N. meningitidis.* Andre *et al.* describe a number of vaccine technologies without highlighting any one technology as being more promising than another is. It is impermissible, within the framework of section 103, to pick and choose from any one reference only so much of it as will support a given proposition, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art. There are no detailed tables, graphs, or protocols concerning meninogococcal vaccine production. (g) Lindberg fails to definitively specify the quantity or quality of any data allegedly considered. The citations in Lindberg are limited to experiences with bivalent A and C meningococcal vaccines and do not

concern the development of efficacious combinations of two, three, or four distinct and separately made protein-capsular polysaccharide conjugates as are presently being claimed. There is no definitive statement in the Lindberg reference as to exactly what Lindberg speculates will be potentially licensed in the future. The mere mention of an as then undeveloped and untested multivalent meningococcal vaccine is an insufficient evidentiary basis for combination with the other cited references.

Applicant's arguments have been carefully considered, but are not persuasive. First, Applicant is reminded that the references of McMaster, Levine *et al*, Andre *et al.* and Lindberg are applied in a rejection under 35 U.S.C. § 103 as opposed to 35 U.S.C. § 102. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In response to Applicant's argument that there is no suggestion to combine the references, the Office recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In the instant case, the suggestion to combine comes from the cited secondary references. The rejection based on the disclosure of Granoff (WO 98/58,670) was withdrawn as indicated via paragraph 13 of the Office Action mailed 12/07/04. Applicant is reminded that the Office is not required to provide rebuttal to Applicant's arguments on a rejection that is moot. Moreover, it is self-evident that despite Granoff's alleged 'conspicuous and significant' omission, McMaster did succeed in making protein-capsular polysaccharide conjugates comprising meningococcal serogroups A, C, W-135 and Y. Nothing in Granoff's disclosure (WO 98/58670) teaches not to combine the four separately made meningococcal capsular polysaccharide-protein conjugates of McMaster. The teachings of McMaster's patent when combined with the disclosure of Andre *et al.*, Levine *et al.*, and Lindberg AA as set forth, provide the *prima facie* evidence that the alleged 'obvious to try' rationale is baseless. Contrary to Applicant's argument, the claims do not require successful administration of multivalent/tetravalent combination of

protein-capsular polysaccharide conjugates comprising meningococcal serogroups W-135 and Y. Moreover, the knowledge in the art at the time of the instant invention indicates that the concept of providing more than one capsular polysaccharides in one vaccine or composition was not novel, but was well within the realm of routine experimentation since the art typically engaged in such experimentation. At the time of the instant invention, Chong *et al.* (WO 99/42130) had already established reasonable expectation of success with a multivalent immunogenic molecule comprising multiple purified capsular polysaccharides or oligosaccharides of *Neisseria meningitidis* derived from serogroup A, C, W-135 and Y, each conjugated to a carrier protein for use as a medicament against meningitis (see claims 1, 6-8, 39 and 40; paragraph bridging pages 9 and 10; pages 10 and 12; and Examples 1, 2 and 4). Bivalent meningococcal capsular polysaccharide or oligosaccharide-protein conjugates were already evaluated for efficacy in the art. See teachings of Costantino *et al.* Adding an additional art-known W-135 or Y conjugate such as McMaster's was well within the realm of what one of skill in the art usually engages in.

The reference of Andre *et al.*, Levine *et al.* or Lindberg is not applied under 35 U.S.C. § 102, and therefore Andre *et al.*, Levine *et al.* or Lindberg do not have to teach detailed tables, graphs, or protocols concerning meninogococcal vaccine production. Lindberg does not have to definitively specify the quantity or quality of any data considered. Andre *et al.* do not have to describe one vaccine technology that is more promising than the other. At the time of the instant invention, the primary reference of McMaster already provided detailed teachings as to how to make the four individual meninogococcal A, C, W-135 and Y capsular polysaccharide conjugates. McMaster was already successful in making individual protein-capsular polysaccharide conjugates comprising meningococcal serogroups W-135 or Y in addition to protein-capsular polysaccharide conjugates of meningococcal serogroups A and C. Combining these conjugates as desired or as described to produce a combination immunological composition would require nothing more than routine experimentation given the explicit motivation to combine such conjugates. Lindberg had already predicted that meningococcal A + C + W135 + Y glycoconjugates will most likely be marketed (see thirds full paragraph in left column on page S34). Because a reasonable expectation of success of such a combined conjugate vaccine was anticipated by those of skill in the art at the time of the invention, Levine *et al.* went to the extent of performing a cost-effectiveness analysis for

routine immunization with a quadrivalent A, C, Y and W-135 meningococcal polysaccharide-protein conjugate vaccine. These are clearly indicative of a reasonable expectation of success with a combination meningococcal A + C + W135 + Y glycoconjugate vaccine. Furthermore, at the time of the instant invention, Chong *et al.* (WO 99/42130) had already established reasonable expectation of success with a multivalent immunogenic molecule comprising multiple purified capsular polysaccharides or oligosaccharides of *Neisseria meningitidis* derived from serogroup A, C, W-135 and Y, each conjugated to a carrier protein for use as a medicament against meningitis (see claims 1, 6-8, 39 and 40; paragraph bridging pages 9 and 10; pages 10 and 12; and Examples 1, 2 and 4). Nothing in the art at the time of the invention suggested a lack of reasonable expectation of success upon combining McMaster's individually produced meningococcal A, C, W135 and Y glycoconjugates as set forth in the rejection. Clearly, the Office has established a *prima facie* case of obviousness. A clear motivation to combine McMaster's individual conjugates, and a reasonable expectation of success are both found in the prior art teachings.

In sum, if each of the applied references taught all the ingredients of the claimed composition, then each of the cited references would have been applied as an anticipatory prior art under 35 U.S.C § 102. Applicant appears to argue that the obviousness rejection fails because there are no anticipatory references teaching the instantly claimed product. It should be noted that what would reasonably have been known and used by one of ordinary skill in the art need not be explicitly taught. '[F]or the purpose of combining references, those references need not explicitly suggest combining teachings, much less specific references'. *In re Nilssen*, 851 F.2d 1401, 1403, 7 USPQ2d 1500, 1502 (Fed. Cir. 1988). The test of obviousness is not express suggestion of the claimed invention in any and all of the references, but rather what the references taken collectively would reasonably have suggested to those of ordinary skill in the art presumed to be familiar with them. *In re Keller*, 642 F.2d 413, 425, 208 USPQ 871, 881 (CCPA 1981). '[T]he question is whether there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination'. *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1462, 221 USPQ 481, 488 (Fed. Cir. 1984). In the instant case, the cited secondary references provide sufficient reason, sufficient suggestion, and/or sufficient motivation to combine the cited teachings. There is express suggestion by secondary prior art

references to combine meningococcal A, C, Y and W-135 conjugates. Obviousness does not require absolute predictability (see *In re Lamberti*, 192 USPQ 278), but only a reasonable expectation of success (see *In re O'Farrell*, 7 USPQ 2d 1673, Fed. Cir. 1988). The Office has clearly established this in the instant application. The rejection stands.

48) The rejection of claims 18-36, 46, 48-51, 56 and 57 made in paragraph 23 of the Office Action mailed 12/07/04 under 35 U.S.C. § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10: 691-698, 1992, already of record) and McMaster (6,146,902 – Applicants' IDS submitted 07/07/04) in view of Andre *et al.* (*In*: *Modern Vaccinology*. (Ed) Kurstak *et al.* Plenum Medical Book Company, New York, pp. 41-54, 1994, already of record); Levine *et al.* (*In*: *Abstracts of the Tenth International Pathogenic Neisseria Conference*, (Ed) Zollinger *et al.* Baltimore, USA, pages 228-230, November, 1997, already of record) and Lindberg AA (*Vaccine* 17: S28-S36, 1999 – Applicants' IDS), is maintained for reasons set forth therein and herebelow.

Applicant submits that: (a) Costantino *et al.* do not teach or suggest combinations of two, three, or four distinct and separately made protein-capsular polysaccharide conjugates, wherein each of the conjugates comprises a purified capsular polysaccharide from *N. meningitidis* serogroup of A, C, W-135 or Y conjugated to a carrier protein, wherein at least one serogroup is W-135 or Y. (b) The Office restricts use of Costantino *et al.* to the argument that adjuvanted bivalent (A and C) meningococcal polysaccharide-protein conjugates were known in the art. Thus, the Office's arguments are only potentially relevant as to claims 34-36 directed to adjuvanted compositions depending upon base claim 18. As the obviousness/non-obviousness of claims 34-36 is tied to the examination of independent claim 18, Applicant reserves further comment on Costantino *et al.* until disposition of claim 18.

Applicant's arguments have been carefully considered, but are not persuasive. Costantino *et al.* was not applied as prior art 35 U.S.C. § 102, but under 35 U.S.C. § 102. Contrary to Applicant's allegation, the independent claim 18 was expressly included in the rejection statement. The presence of an adjuvant is not excluded from the scope of claim 18. Instead, the open claim language 'comprising' allows the inclusion of any other substance other than the recited conjugates, including an adjuvant. Applicant has failed to advance substantive arguments with regard to Costantino *et al.* and with regard to the 103 rejection of record as a whole. The rejection stands.

49) The rejection of claims 52 and 54 made in paragraph 26 of the Office Action mailed 12/07/04 under 35 U.S.C. § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10: 691-698, 1992, already of record) and McMaster (6,146,902 - Applicants' IDS submitted 07/07/04) as modified by Andre *et al.* (*In*: *Modern Vaccinology*. (Ed) Kurstak *et al.* Plenum Medical Book Company, New York, pp. 41-54, 1994, already of record), Levine *et al.* (*In*: *Abstracts of the Tenth International Pathogenic Neisseria Conference*, (Ed) Zollinger *et al.* Baltimore, USA, pages 228-230, November, 1997, already of record) and Lindberg AA (*Vaccine* 17: S28-S36, 1999 – Applicants' IDS) as applied to claim 51, 33 and 18 above, and further in view of Avendano *et al.* (*Pediatric Infect. Dis. J.* 12: 638-643, 1993), is maintained for reasons set forth therein and herebelow.

Applicant argues that: (a) Avendano *et al.* teach the concomitant administration of PRP-T and DTP using a single syringe for deep subcutaneous inoculations. (b) The reference does not teach or suggest the concomitant administration of any type/number of capsular polysaccharide-protein glycoconjugates in a single syringe. (c) The reference is silent with respect to the concomitant administration of any one or more of the presently claimed *N. meningitidis* capsular polysaccharide-protein conjugates.

Applicant's arguments have been carefully considered, but are not persuasive. Applicant is reminded that Avendano *et al.* is not applied as an anticipatory art, but is applied as a secondary reference under 35 U.S.C. § 103 in combination with the teachings of Costantino *et al.* and McMaster as modified by Andre *et al.*, Levine *et al.* and Lindberg AA. Avendano's teachings are directly pertinent to what is claimed in the instant claims as set forth in paragraph 26 of the Office Action mailed 12/07/04. The rejection stands.

Rejection(s) under 35 U.S.C. § 112, First Paragraph (New Matter)

50) Claim 35 and those dependent therefrom are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The added limitations 'saponin' and 'QG-21' in claim 35, as amended, are new matter. Claim 35, as amended, further includes the added limitations: '(N-2-Deoxy-2-L-leucylamino

.....hydroacetate', '(3-.....cholesterol)', 'Poly[bis(carboxylatophoxy)phosphazene] and/or Poly[di(carboxyatophoxy)phosphazene])', which constitute new matter. There is no descriptive support in the specification, as originally filed for the above-identified new limitations. Therefore, the above-identified limitations in the claims are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicant is respectfully requested to remove the new matter from the claim(s), or point to specific pages and line numbers in the originally filed specification where support for the above-identified limitations can be found.

51) Claim 49 is rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 49 includes the broad limitation: 'inactivated bacterial toxin is derived from *Corynebacterium diphtheriae'*. However, the descriptive support in the specification as originally filed is limited to only two inactivated bacterial toxins from *Corynebacterium diphtheriae,* i.e., diphtheria toxoid and CRM197 (see lines 9-11 on page 5). No other inactivated bacterial toxin derived from *Corynebacterium diphtheriae* is supported in the specification, as originally filed. The full scope of the broad limitation 'inactivated bacterial toxin is derived from *Corynebacterium diphtheriae'* is not supported by the instant specification. Therefore, the above-identified limitation in the claim is considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicant is respectfully requested to remove the new matter from the claim(s), or point to specific pages and line numbers in the originally filed specification where support for the above-identified limitation can be found.

52) Claims 46 and 48 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject

matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 46 and 48 include the broad limitation: 'single protein species'. However, the descriptive support in the specification as originally filed is limited to a 'single carrier protein species' (see paragraph 0026). The full scope of the broad limitation 'single protein species' is not supported by the instant specification. Therefore, the above-identified limitation in the claims is considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicant is respectfully requested to remove the new matter from the claim(s), or point to specific pages and line numbers in the originally filed specification where support for the above-identified limitation can be found.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

53) Claims 18-36, 46, 48-52, 54, 56 and 57 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite, for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

(a) Claim 18 is incorrect and/or confusing in the recitation: 'capsular polysaccharide from *N. meningitidis* serogroup of A, C, W-135 or Y', because the capsular polysaccharide can be from *N. meningitidis* belonging to a specific serogroup, but cannot be from *N. meningitidis* serogroup. For the purpose of distinctly claiming the subject matter, it is suggested that Applicant replace the above-identified phrase with: --capsular polysaccharide from *N. meningitidis* of serogroup A, C, W-135 or Y--.

(b) Claim 22 is vague, indefinite, lacks proper antecedent basis and/or improperly broadening in scope in the limitation: 'protein-polysaccharide conjugates'. Claim 22 depends from claim 18 which includes a narrower limitation, --protein-capsular polysaccharide conjugates--, but not 'protein-polysaccharide conjugates'.

(c) In claim 22, for the purpose of distinctly claiming the subject matter, it is suggested

that Applicant replace the limitation: 'comprising a combination of two distinct ..... conjugates, wherein a first conjugate comprises .... a second conjugate comprises' with the limitation: --wherein said immunological composition comprises ... first conjugate comprising ..... second conjugate comprising--.

(d) Claim 22 is vague and/or lacks proper antecedent basis in the limitation: 'a first conjugate comprises a purified capsular polysaccharide of *N. meningitidis* serogroup W-135 and a second conjugate comprises a purified capsular polysaccharide selected from the group consisting of *N. meningitidis* serogroups Y, A and C'. The limitations 'a first conjugate' and 'a second conjugate' should be replaced with the limitations --the first conjugate-- and --the second conjugate-- respectively, since a combination of two conjugates cannot have more than one first conjugate and more than one second conjugate.

(e) Claim 35 is indefinite and confusing in the use of the improper Markush claim language: 'selected from the group consisting of ..... and/or .... and'. When materials recited in a claim are so related as to constitute a proper Markush group, they may be recited in the conventional manner, or alternatively. For example, if 'wherein R is a material selected from the group consisting of A, B, C **and** D' is a proper limitation; 'wherein R is a material selected from the group consisting of A, B, C or D' is an improper limitation.

(f) Claim 22 is vague, indefinite, confusing and/or incorrect in the limitation: 'capsular polysaccharide selected from the group consisting of *N. meningitidis* serogroups Y, A and C' (see last two lines), because the Markush species as presented represent *N. meningitidis* bacteria, not capsular polysaccharides. For the purpose of distinctly claiming the subject matter, it is suggested that Applicant replace the limitation with --*N. meningitidis* capsular polysaccharide selected from the group consisting of serogroups Y, A and C--.

(g) Claim 23 is indefinite and/or lacks proper antecedent basis in the limitation 'a purified capsular polysaccharide .... serogroup Y'. Claim 23 depends from claim 22 which already recites a purified capsular polysaccharide of serogroup Y. For proper antecedence, it is suggested that Applicant replace the limitation with --the purified capsular polysaccharide ..... serogroup Y--.

(h) Analogous criticism and rejection apply to claims 24, 25, 27-29 and 33.

(i) Claim 29 is vague, indefinite and confusing in the limitation 'capsular

polysaccharide selected from the group consisting of Y, A and C' (see lines 5 and 6) which limitation is further inconsistent with the Markush language 'capsular polysaccharide selected from the group consisting of serogroup Y, A and C' (see lines 6 and 7).

(j) Claims 30-32 are indefinite and incorrect in the limitation: 'composition of claim 29, wherein at least one of the second conjugate', because claim 29, from which claims 30-32 depend, does not recite more than one second conjugate. Note that the term 'at least' has no upper limit. With regard to the second conjugate, the scope of claims 30-32 is indeterminate.

(k) Claim 35 is vague and indefinite in the limitation "QG-21", because it is unclear what does this limitation represent.

(l) Claim 35 is vague, indefinite and confusing in the limitation "pcpp", because it is unclear how the limitation "pcpp" can represent both 'Poly[bis(carboxylatophoxy)phosphazene *and* Poly[di(carboxylatophoxy)phosphazene)' [Emphasis added].

(m) Claim 35 is vague and indefinite in the limitation 'oligodeoxynucleotide motifs "CpG", because it is unclear how the limitation "CpG" can be referred to as 'oligodeoxynucleotide motifs'. The art appears to refer to 'oligodeoxynucleotide motifs' by the abbreviation 'ODN'. For example, see paragraph [0218] of US 20050208605.

(n) Claim 51 is vague in the limitation: 'immunological composition of claim 33 formulated as a sterile liquid'. For the purpose of distinctly claiming the subject matter, it is suggested that Applicant replace the limitation with --immunological composition of claim 33, wherein the composition is formulated as a sterile liquid--.

(o) Claim 56 is indefinite and incorrect in the use of the improper Markush limitation: 'selected from the list consisting of'. For the purpose of distinctly claiming the subject matter, it is suggested that Applicant replace the limitation with --selected from the group consisting of--.

(p) Claims 46 and 48 are indefinite because the limitation 'single protein species' is improperly broadening in scope compared to the earlier limitation 'carrier protein' in claim 46. To be of consistent scope, it is suggested that Applicant replace the limitation 'single protein species' in both claims with the limitation --single carrier protein species-- as is supported in paragraph [0026] of the originally filed specification.

(q) Claims 19-36, 46, 48-52, 54, 56 and 57, which depend directly or indirectly from

claim 18, are also rejected as being indefinite because of the indefiniteness identified above in the base claim.

Objection(s)

54) The extra space between the period and the last limitation 'serogroup A .' is objected to.

Remarks

55) Claims 18-36, 46, 48-52, 54, 56 and 57 stand rejected.

56) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of amendments, responses or papers is (571) 273-8300.

57) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

58) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

August, 2005

S. DEVI, PH.D.
PRIMARY EXAMINER